



PATENT
Customer Number: 22,852
Attorney Docket No. 02481.1718.00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Uwe HEINELT *et al.*

Application No.: 09/734,008

Filed: December 12, 2000

For: SUBSTITUTED
NORBORNYLAMINO
DERIVATIVES, PROCESSES
FOR THEIR PREPARATION,
THEIR USE AS
MEDICAMENTS OR
DIAGNOSTICS, AND A
MEDICAMENT COMPRISING
THEM

Group Art Unit: 1626

Examiner: E. Sackey

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. § 1.116

The final Office Action of September 24, 2003, has been received and its contents carefully considered. Reconsideration of the rejections is respectfully requested in view of the following remarks. This response is due by December 24, 2003, and is timely filed.

I. Status of the Application and Claims

Claims 1-50 are pending in this application. The Office has rejected claims 1-3, 25, and 26. The Office has objected to the remaining claims, 4-24 and 27-50, as being

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dependent upon a rejected base claim, but has indicated that they "would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." (Office Action at 6.)

II. Bondavalli Does Not Anticipate Applicants' Claim 1

The Office has maintained the rejection of claim 1 under 35 U.S.C. § 102(b) as being anticipated by F. Bondavalli *et al.*, "Synthesis and Pharmacological Activity of Derivatives of Exo-trimethylenenorbornane," *Il Farmaco - Edizione Scientifica*, Vol. 34, No. 11 (Nov. 1979), pp. 945-51 (hereinafter referred to as "Bondavalli"). (Office Action at 2.) Applicants traverse the rejection.

In the Office Action mailed April 17, 2003, the Office states that "Applicants claim a substituted norbornylamino compound of formula (I) and (Ia)" and that Bondavalli "discloses a substituted norbornylamino compound which is identical to the instantly claimed compound. See Table II, compound (Vd) on page 949." (April 17, 2003, Office Action at 3.)

In Applicants' Request for Reconsideration submitted July 14, 2003 (hereinafter referred to as "Response"), it was explained that claim 1 "covers a genus of chemical compounds" and that "[e]ach of the compounds in that genus has as an element an 'exo-configured nitrogen.'" (Response at 2.) Applicants further explained that because the compounds of Bondavalli, including compound (Vd) cited by the Office, have an endo-configured nitrogen, Bondavalli does not anticipate claim 1. (*Id.* at 3.)

Furthermore, in the final Office Action, the Office has recognized that Bondavalli "discloses what appears to be an endo-nitrogen as compared to the required exo-

nitrogen" (Office Action at 5), which compels a finding of no anticipation as a matter of law.

The Office has not offered any explanation of why Appellants' arguments are unpersuasive. The Office is required to "clearly stat[e] the reasons in support" of a final rejection. 37 C.F.R. § 1.113(b). Moreover, "the examiner should . . . take note of the applicant's argument *and answer the substance of it.*" M.P.E.P. § 707.07(f) (8th ed., revision 1, Feb. 2003) (emphasis added). The Office has not done so. Accordingly, on the basis of the Response, Applicants respectfully request that the Office reconsider claim 1 and withdraw this rejection.

III. Bondavalli Does Not Render Any of Applicants' Claims Obvious

The Office has maintained the rejection of claims 2, 3, 25, and 26 under 35 U.S.C. § 103(a) as being unpatentable over Bondavalli. (Office Action at 2.) Applicants traverse the rejection.

The Office states that it was not persuaded "with regards to applicants['] claim of an exo-nitrogen compound of claim 1, because the reference broadly teaches an exo-trimethylenenorbornane compound of formula (I). See [T]able II, compound Vd." (*Id.* at 3.) For the reasons set forth above, Applicants have shown that compound (Vd) is not a "compound of formula (I)."

The Office mentions the term "exo-trimethylenenorbornane" in the context of Bondavalli's alleged teaching. (*Id.*) It is important to recognize, however, that the "exo" prefix of that term refers to the five-membered ring of the molecules in Bondavalli, not the amino nitrogen atom, which in Bondavalli is in the "endo" configuration. (See

Bondavalli at 948-49 (entitling Tables I and II as, respectively, "Amides of exo-5,6-

trimethylenenorbornan-2-endo-amine (IV a-g)" and "N-substituted exo-5,6-trimethylenenorbornan-2-endo-amines (V a-f)"). Applicants' claims recite compounds having exo-configured nitrogen atoms.

The Office also relies on homology and cases discussing that principle in the context of compound claims. (Office Action at 3-4.) Specifically, the Office cites *In re Druey*, 138 U.S.P.Q. 39 (C.C.P.A. 1963), and *In re Payne*, 203 U.S.P.Q. 245, 255 (C.C.P.A. 1979), as supporting the rejection. The Office also states that it "disagrees with the assertion that [compound (Vd)] was chosen to support a given position." (Office Action at 3.) Applicants observe, however, that no compound other than compound (Vd) was mentioned in the April 17, 2003, Office Action. Furthermore, as Applicants have explained, the threshold issue in this case is whether there is motivation to select compound (Vd) (or any other compound in Bondavalli) and then modify that compound to obtain a compound within the scope of Applicants' claims. (Response at 4-5 (citing *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 56 U.S.P.Q.2d 1641, 1645 (Fed. Cir. 2000)).) The Office has not addressed either Applicants' argument on this issue or the impact of the *Yamanouchi* decision on the present case.

And neither *Druey* nor *Payne* supports the rejection of the Applicants' claims. In *Druey*, the required motivation was present in the prior art, which taught the same utility as the claimed compound (that is, as intermediates for sulfa drugs). 138 U.S.P.Q. at 40. In *Payne*, a utility of pesticidal activity was disclosed, which was also the disclosed use of the claimed compounds. 203 U.S.P.Q. at 248. As explained by Applicants in the Response, no utility is shown for compound (Vd). (Response at 6-7.)

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The Office's citation (Office Action at 4) of *In re Gyurik*, 201 U.S.P.Q. 552, 557 (C.C.P.A. 1979), does not support its rejection of Applicants' claims. The quotation from that case regarding the "expectation that compounds similar in structure will have similar properties," does not meet the threshold issue discussed above, that is, there must be motivation to choose the prior art compound before the presence or absence of similarity in chemical structure even becomes relevant. In *Gyurik*, the prior art compounds possessed the same utility as the claimed compounds. 201 U.S.P.Q. at 553-54. That is not the situation here. On this point, Applicants cited (Response at 4, 6) the M.P.E.P. and *In re Sterniski*, 170 U.S.P.Q. 343 (C.C.P.A. 1971). The *Sterniski* court observed:

Where the prior art reference neither discloses nor suggests a utility for certain described compounds, why should it be said that a reference makes obvious to one of ordinary skill in the art an isomer, homolog or analog of related structure, when that mythical, but intensely practical, person knows of no 'practical' reason to make the reference compounds, much less any structurally related compounds?

170 U.S.P.Q. at 347. Under *Sterniski* and *Yamanouchi*, the Office has the burden of showing the "practical" reason that one of ordinary skill in the art would have (1) selected a compound from the several compounds listed in Bondavalli and (2) then modified it to obtain one of the compounds the Applicants have invented. The Office has not done so.

The Office recognizes that the Bondavalli compounds have endo-configured nitrogen atoms. (Office Action at 4-5). It then states that "there is nothing of record by way of unexpected results or properties that would obviate the *prima facie* case of obviousness." (*Id.* at 5.) But for the reasons shown above, Applicants submit there is

no *prima facie* case to rebut because there is no motivation to select the amine compounds for the reasons set forth in Applicants' Response. (Response at 6-7.)

The Office then states that Applicants "have not stated that the endo-amine does not possess any utility." (09/24/03 Office Action at 5.) But Applicants did in fact make that point in their Response. (Response at 6-7 ("[T]he compound relied upon by the Office, compound (Vd), is an amine that was not even tested at all for utility") ("The only amine tested in Bondavalli, compound (Vf), . . . did not exhibit useful CNS or anticonvulsant activity.")). Moreover, the Office has the initial burden of establishing a *prima facie* case, including utility in the prior art, but it has not done so here.

The Office further observes that Bondavalli does "not state that there would be equivalent utility if the nucleus of the molecule is changed from an endo-nitrogen to an exo-nitrogen or vice versa." (Office Action at 5.) That observation supports the patentability of the Applicants' claims, not their rejection. Bondavalli provides no motivation to make molecules having exo-configured nitrogen atoms, nor does it provide any expectation that any such compounds would have any useful properties.

The Office states that Bondavalli "does not have to test all compounds for all utilities." (09/24/03 Office Action at 5.) But *Stemniski* shows that the prior art must show *some* utility for the compound the Office relies upon to make an obviousness rejection, because it is not obvious to modify a compound having no known utility. Bondavalli does not show that the endo-amine compounds have any useful property; indeed, the sole amine compound tested produced a harmful effect, as Applicants have previously explained. (Response at 7.)

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The Office's approach essentially focuses on the general teachings of Bondavalli that the amide compounds have utility, without taking into account the more relevant specific teachings of Bondavalli that the tested amine compound showed no utility. *See, e.g., In re Lunsford*, 148 U.S.P.Q. 721, 724 (C.C.P.A. 1966) ("The specific teachings . . . are closely concerned with the claimed invention. Absent any reason to the contrary, it is these teachings which a person of ordinary skill in the art would consider most pertinent and accord the most weight."). In this case, when Bondavalli is considered as a whole, its specific teachings suggest that the endo-amine compounds are not useful. And if the endo-amine compounds are not useful, why would the person of ordinary skill in the art be motivated to make the exo-amine compounds recited in the claims?

The Office's statement regarding method claims 25 and 26, that "there is nothing on record to show unobvious properties between compound Vd and applicants'[] claimed compound," again presupposes the existence of a *prima facie* case that Applicants submit does not exist. Furthermore, there is no evidence in the record that the compounds of Bondavalli would be useful in treating or preventing ischemic states of the peripheral nervous system or the central nervous system, which provides yet another basis for the conclusion that no *prima facie* case exists here with respect to claims 25 and 26.

Even so, there is evidence of unexpected results in the record. The specification shows that compounds having an endo-configured nitrogen (Examples 7 and 8) are less active than a corresponding compound (Example 9) having an exo-configured nitrogen.

(*See* "NHE3 activity" table, Specification at 56.) Although this comparison does not

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(See "NHE3 activity" table, Specification at 56.) Although this comparison does not

involve compound (Vd) of Bondavalli cited by the Office, it still suffices to show that the configuration of the nitrogen is important and leads to unexpectedly different activity. See *In re Foster*, 145 U.S.P.Q. 166, 175-76 (C.C.P.A. 1965) (reversing rejection of two claims for unexpected results, even though the closest prior art polymer was not part of comparative testing).

When claims 2, 3, 25, and 26 are properly construed and Bondavalli is properly evaluated, the compelled result is a holding of nonobviousness for the reasons set forth above. Therefore, Applicants respectfully request that the Office reconsider those claims and withdraw the rejection.

IV. Conclusion

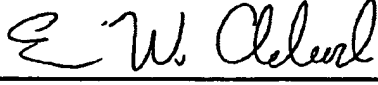
In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: December 23, 2003

By: 
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